Ten Years of MS/MS Screening at the Northwest Newborn Screening Program

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Testing done at the Oregon State Public Health laboratories in Hillsboro Oregon

The Northwest Newborn Screening Program (NWRNBS)

began Newborn Screening in 1963. This year marks our 51st year of providing Newborn Screening service. The NWRNBS program began MS/MS (Tandem Mass Spectrometry) screening in October 2002. We have added several disorders and their analytes to our screening panel since then and now use 49 analytes and ratios to screen for 26 disorders by MS/MS. We will present ten years of data in this poster. From July 1, 2004 thru June 30, 2014 we tested 1,625,529 infants.

The NWRNBS has provided Newborn Screening, Follow-up and Medical Consultation for Alaska, Hawaii, Idaho, the Navajo Nation, Nevada, New Mexico, Oregon, Military bases, Guam, and Saipan. Nevada left the program on July 1, 2014 to start testing their specimens in Nevada.

We began testing in October 2002 using the Perkin Elmer derivitized Neogram Mass Spec Assay and a Sciex mass spectrometer. We changed to Quatro Micro mass spectrometers in January 2008.

We changed to the Perkin Elmer non-derivitized Neobase MS/MS assay in June 2010. We added SUAC testing January 2011. SUAC could not be added to the assay until the assay was changed to the non-derivitized assay. This made Tyrosinemia Type I much easier to detect, eliminated false negative elevations of tyrosine and prevented many false positives from having diagnostic testing. We changed to the TQD mass spectrometer in December 2013. The TQD Mass Spec has easier maintenance and is more sensitive than the Quatro Micro Mass Spec.

Most of the disorders are found on the first specimens. Some disorders have been found only on the first specimens, such as VLCAD. The C14:1 is elevated on the first specimen, but not on the second specimen. A normal C14:1 result on a second specimen does not rule out VLCAD. Diagnostic testing is needed on all infants who have an elevated C14:1 on the first specimen.

Some disorders we find mostly on the second specimens, such as Tyrosinemia Type II and Homocystinuria. Since Oregon requires two routine specimens, we have a second chance to find disorders with a delayed analyte elevation.

- Using Tandem Mass Spec we detected 431 confirmed cases or one case in 3,771 infants.
- Fatty Acid Oxidation Disorders occurred one case in 8,739 infants.
- Amino Acid Disorders occurred in one case in 11,694 infants.
- Organic Acidemia Disorders occurred one case in 15,335 infants.
- In ten years the NWRNBS Lab tested 1,625,529 infants.

Amino Acid Disorders

Amino Acid Disorders	Cases	One case in:	Analytes	Ratios
All cases	139	**11,649**	Amino Acids	
ARG Arginase deficiency	1	1,625,529	Arg	
ASA Arginosuccinic Acidemia	13	125,041	ASA	
CIT Citrullinemia	5	325,106	Cit	
MSUD Maple Syrup Urine Disorder	6	270,922	Leu	Leu/Ala
HCY Homocystinuria	8	203,191	Met	
MET Hypermethionemia	15	108,369	Met	
MAT Methionine Adenosyl Transferase	3	541,843	Met	
PKU Phenylketonuria	57	28,518	Phe	Phe/Tyr
H-PHE Hyperphenylalanemia	27	60,205	Phe	
TYR I Tyrosinemia Type 1	2	812,765	SUAC, Tyr	
TYR II Tyrosinemia Type 2	2	812,765	Tyr	

We find many NICU infants with amino acid elevations due to TPN. We find elevations of Leu, Met, Phe, Tyr, C5 and C3DC_C4OH. We request another blood spot sample for follow-up.

Waters TQD Mass Spec.

Fatty Acid Oxidation Disorders

Fatty Acid Oxidation Disorders	Cases	One case in:	Analytes	Ratios
All cases (except CPT1 Arctic cases)	186	**8,739**	C0 thru C18OH	
CUD Carnitine Uptake/ Transport Defect	14	116,109	Low C0	
CPT1 Carnitine Palmitoyl Transferase	2	812,765		C0/(C16+C18)
CPT1 Arctic variant	737	150 Alaska Infants		C0/(C16+C18)
CPT1 Pacific Islander variant	9	20,925 Hawaii infants		C0/(C16+C18)
CPTII Carnitine Palmitoyl Transferase 2	4	406,382	C16, C18, C18:1	
SCAD Short Chain Acyl CoA Deficiency	20	81,276	C4	
MCAD Medium Chain Acyl CoA Def.	85	19,124	C8, C10, C6, C10:1	C8/C10
VLCD Very Long Chain Acyl CoA	26	62,520	C14:1, C14, C14:2	
VLCAD DNA 1226 mutation Hawaii	15	108,369	C14:1, C14, C14:2	
TFP Tri Functional Protein Defect	5	325,106	C14:1, C14, C14OH, C16OH, C16:1OH	
TYR II Tyrosinemia Type 2	2	812,765	Tyr	
LCHAD Long Chain Hydroxyl CoA	3	541,843	C16OH, C18OH, C18:1OH, C16:1OH	
MADD Multiple Acyl CoA Dehydrogenase Deficiency	3	541,843	C10, C8, C6, C14, C14:1, C16:1	

Fatty Acid Oxidation Disorders occurred one case in 8,883 infants. This excludes the many hundreds of CPT1 Arctic variant cases found on Alaska specimens.

CPT1 Arctic variant cases were found one case in 150 Alaska infants and we know we are not finding all of them by MS/MS. We plan on going to DNA testing for the Arctic variant on Alaska specimens.

We also found 9 cases of CPT1 (one case in 20,925 infants) from Pacific Island people living in Hawaii. The mutation is different from the classic CPT1 and the Arctic Variant.

From Hawaiian infants we found 15 cases of VLCAD DNA Mutation 1226 for one case in 12,555 Hawaii infants.

Organic Acidemias

Organic Acidemias	Cases	One case in:	Analytes	Ratios
All cases	106	**15,335**	C3 thru C6OH	
PA Proprionic Acidemia	6	270,922	C3	C3/C2
MMA Methylmalonic Acidemia	17	95,619	C3	C3/C2
Cbl C Cobalamine C	5	325,106	C3	C3/C2
MA Malonic Acidemia	zero	na	C3DC_C4OH	C3DC_C4OH/C10
IBD Isobutyral CoA Dehydrogenase	1	1,625,529	C4	See SCAD also
GA II Glutaric Acidemia Type 2	zero	na	C4, C5, C6, C8, C10	See MADD also
3MCC 3-Methylcrotonyl CoA Carboxylase	32	50,798	C4DC-C5OH	
MCD Multiple Carboxylase Def.	2	812,765	C4DC-C5OH	
HMG 3-Hydroxy-3-methylglutaryl-CoA	1	1,625,529	C4DC-C5OH	
3MGA 3-Methylglutaconic Acidemia	zero	na	C4DC-C5OH	
IVA Isovaleric Acidemia	11	147,775	C5	
2MBCD 2-Methyl-butyryl CoA Def.	9	180,614	C5	
2M3HBA 2-Methyl-3-Hydroxybutiric	3	541,843	C5:1, C4DC_C5OH	
BKT Beta Ketothiolase Deficiency	zero	na	C5:1, C4DC_C5OH	
GA I Glutaryic Acidemia Type 1	19	85,544	C5DC-C6OH	C5DC-C6OH/ C8 or C5DC-C6OH /C16

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